

DOCKET NO: 250307US0DIV

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF :
MASAHIRO KAKEHI, ET AL. : EXAMINER: E. SLOBODYANSKY
SERIAL NO: 10/798,339 :
FILED: MARCH 12, 2004 : GROUP ART UNIT: 1652
FOR: METHOD FOR PRODUCING NUCLEOTIDE BY FERMENTATION

REPLY BRIEF

COMMISSIONER FOR PATENTS
ALEXANDRIA, VIRGINIA 22313

SIR:

This is a reply to the Examiner's Answer dated April 4, 2008.

The claimed invention is a method for producing a specified nucleoside 5'-phosphate ester. The method is based on the discovery that decreasing expression of the *ushA* and *aphA* genes by mutating or disrupting those genes substantially eliminates the 5'-nucleotidase activity in the periplasm of *E. coli*. As a result, inosine 5'-phosphate ester and guanosine 5'-phosphate ester are produced at improved yields as compared to wild-type *E. coli*.

The claimed method is not obvious because the cited references, Thaller et al., Cowman et al. and Matsui et al., taken in combination, fail to suggest that decreasing expression of the *ushA* and *aphA* genes by mutating or disrupting those genes would substantially eliminate the 5'-nucleotidase activity in the periplasm, as claimed. Therefore, that result would not have been predicted from the cited references and establishes the non-obviousness of the claimed method.

No evidence has been provided by the Office to support the Examiner's assertion that one of ordinary skill in the relevant field in relevant timeframe would have predicted that decreasing expression of the *ushA* gene and the *aphA* gene by mutating or disrupting those genes would substantially eliminate the 5'-nucleotidase activity in the periplasm, as claimed. As stated by the Supreme Court in KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007):

The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield **predictable results**.

When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a **predictable variation**, §103 likely bars its patentability.

Sakraida and Anderson's-Black are illustrative-a court must ask whether the improvement is more than **predictable use of prior art elements** according to their established functions.

82 USPQ2d 1395, emphasis added.

In the absence of such evidence, the rejection cannot be sustained.

In view of the foregoing, the claimed method is not obvious in view of Thaller et al. Cowman et al. and Matsui et al. Accordingly, the rejection under 35 U.S.C. §103(a) should be reversed.

Respectfully submitted,

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